

### **REMARKS**

The Office Action of May 19, 2009, has been carefully studied. Claims 25-28 and 35 currently appear in this application. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicant respectfully requests favorable reconsideration and formal allowance of the claims.

### **INTERVIEW SUMMARY**

Applicant's attorney wishes to thank Examiner Peselev for the courtesies extended during the telephone interview of August 17, 2009. During that telephone interview, Examiner Peselev authorized submission of a supplemental amendment in the present application.

This supplemental amendment is submitted to correct self-evident typographical errors in the amendment filed July 24, 2009.

### **Amendments**

Claims 25 and 35 have been amended to introduce the definition of Crystal Form E. Claims 26 and 28 have been amended to introduce the phrase "Crystal Form of", before the phrase "a hemifumarate" in order to make the claims more clear. Support for this amendment can be found in the specification as filed at paragraph 0053.

Claim 27 and the specification of paragraph 0053 have been amended to delete “that contains tetrahydrofuran”, as tetrahydrofuran is not used in obtaining Crystal Form E, as disclosed in paragraphs 0054 and 0119 in the specification as filed. Therefore, one skilled in the art reading the specification at paragraph 0053 will recognize this as an inadvertent typographical error, which the present amendment corrects. It is respectfully submitted that this amendment does not introduce new matter, as it is clear from paragraphs 0054 and 0119 that Crystal Form E does not contain tetrahydrofuran.

The remaining amendments are to correct self-evident typographical errors.

### **Art Rejections**

Claims 28 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Miura et al., US 5,959,088. The Examiner’s position is that Hirade et al., Published Application 2003/0191296, states at paragraph 0040 that the D-type crystal prepared via the E-type crystal ensures a residual solvent content of 1500 ppm or below, which could not be achieved by the prior art D-type crystal and, at paragraph 0042, that the D-type crystal with a large average particle size could not be obtained by the prior art process. The Examiner concedes that Hiraide does not provide a

comparison of the residual solvent content and particle size of the claimed Form D and the Form D disclosed by Miura. The Examiner further states that the stability testing in Miura of the Crystal Form D teaches that Crystal Form D was known in the art at the time of the claimed invention.

This rejection is respectfully traversed.

As shown below, Table 1 of Hiraide discloses Crystal Form D prepared by Examples 2 to 8 and Comparison Examples 1 and 2.

TABLE 1

|                         | Percentage<br>of water<br>(%) | Prepared via<br>E-type crystal | Conditions for conversion<br>of E-type crystal into<br>D-type crystal | Drying conditions                 | Content of<br>residual solvent<br>(ppm) | Particle size<br>( $\mu$ m) | Tabletting<br>troubles |
|-------------------------|-------------------------------|--------------------------------|-----------------------------------------------------------------------|-----------------------------------|-----------------------------------------|-----------------------------|------------------------|
| Example 2               | 2.4                           | Completely                     | 15° C., 3 hr $\rightarrow$ -10° C.                                    | Reduced pressure<br>60° C., 8 hr  | 78                                      | 302                         | —                      |
| Example 3               | 2.6                           | Completely                     | 15° C., 6 hr $\rightarrow$ -10° C.                                    | Reduced pressure<br>60° C., 8 hr  | —                                       | 197                         | —                      |
| Example 4               | 2.0                           | Partially                      | 15° C., 1 hr $\rightarrow$ -10° C.                                    | Reduced pressure<br>60° C., 28 hr | 988                                     | 141                         | No                     |
| Example 5               | 2.0                           | Partially                      | 15° C., 1 hr $\rightarrow$ -10° C.                                    | Reduced pressure<br>60° C., 10 hr | 845                                     | 197                         | No                     |
| Example 6               | 2.0                           | Partially                      | 13° C., 0.5 hr $\rightarrow$ -10° C.                                  | Reduced pressure<br>60° C., 9 hr  | 1049                                    | —                           | —                      |
| Example 7               | 2.0                           | Partially                      | 15° C., 1 hr $\rightarrow$ -10° C.                                    | Reduced pressure<br>60° C., 6 hr  | 647                                     | 163                         | No                     |
| Example 8               | 2.0                           | Partially                      | 15° C., 1 hr $\rightarrow$ -10° C.                                    | Reduced pressure<br>60° C., 10 hr | 893                                     | 185                         | No                     |
| Comparison<br>Example 1 | 1.5                           | Not                            | —                                                                     | Reduced pressure<br>60° C., 16 hr | 2228                                    | 82                          | Yes                    |
| Comparison<br>Example 2 | 1.5                           | Not                            | —                                                                     | Aeration<br>45° C., 20 hr         | 1610                                    | 61                          | Yes                    |

According to the above Table 1, Crystal Form E was not detected in a process of Comparison Examples 1 and 2 in which ethyl acetate containing 1.5% water was used. Miura, US 5,959,088, used a mixture of 1.5 ml water and 100 ml ethyl acetate in Example 8, lines 4-6. Comparing the process of

the above Comparison Examples with that disclosed in Miura, ethyl acetate containing 1.5% water was commonly used in the processes recited in Table 1 and in Miura. Therefore, Crystal Form E was not formed in a process of preparing Crystal Form D disclosed in Miura, as well as in the process disclosed in Comparison Examples 1 and 2 of Table 1 above. Taking the foregoing into consideration, the process and Crystal Form D produced thereby disclosed in Comparison Examples 1 and 2 correspond to the process and Crystal Form D produced and thereby disclosed in Miura.

On the other hand, in the processes of Examples 2 and 8 of the above Table 1, Crystal Form E was detected in the process of preparing Crystal Form D. Crystal Form D was also prepared via Crystal Form E in the presently claimed process. Taking the foregoing into consideration, the processes and the Crystal Form D produced thereby disclosed in Examples 1-8 correspond to the process claimed herein and Crystal Form D produced thereby.

According to Hiraide, Crystal Form D obtained via Crystal Form E has a residual solvent content of 78, 988, 845, 1049, 647 or 893 ppm and a particle size of 302, 197, 141, 197, 163 or 185 microns. On the other hand, Crystal Form D obtained without forming Crystal Form E has a residual solvent content of 2228 or 1610 ppm and a particle size of 82 or

61 microns. It can thus readily be seen that the Crystal Form D claimed herein is different from the Crystal Form D disclosed in Miura in both the amount of residual solvent content and the particle size.

In light of the above, it is respectfully submitted that Crystal Form D, which is obtained from Crystal Form E by the process recited in the present claims, is novel over Crystal Form D that is not obtained via Crystal Form E and disclosed in Miura.

In the present application, the Crystal form D produced by the process claimed herein differs from the Crystal form D disclosed in Miura both in particle size and in the amount of residual solvent. Therefore, the Crystal Form D produced by the process claimed herein is different from the prior art Crystal Form D.

The Federal Circuit, in *Abbott Laboratories v. Sandoz Inc.*, 90 USPQ2d 1769 (Fed. Cir. May 18, 2009), noted that the plaintiff, Abbott, could not capture product obtained by or a product obtainable by processes other than those explicitly recited in the claims [1779]. That is, the process by which the product is obtained limits the claims. In the present application, the process by which the product that is made produces a product that is different from that in the cited prior art, and

therefore the process by which the product is obtained defines over the cited prior art.

Claims 8-11, 25-28 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miura in view of Spanton et al., US 5,945,405.

This rejection is respectfully traversed.

Claims 8-11 have been cancelled, so this rejection is moot with respect to claims 8-11.

Claims 25-28 and 35 have been amended to limit the claims to Crystal Form D and a process for preparing Crystal Form D. Since there are no claims to G Form crystals, it is believed that this rejection is now moot.

Claims 16-18, 23, 25 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miura in view of Spanton and further in view of Bosch. US 6,504,017.

This rejection is respectfully traversed.

Claims 16-18 have been cancelled and claim 23 had previously been cancelled.

The following is a quotation of the third paragraph of MPEP section 2145:

Rebuttal evidence may also include evidence that the claimed invention yields unexpectedly improved properties or properties not present in the prior art.

According to Table 1 of Hiraide, in Crystal Form D obtained from Crystal Form E, the amount of residual solvent is much greater than in Crystal Form D that is not obtained from Crystal Form E. Furthermore, the properties of Crystal Form D obtained from Crystal Form E lead to an avoidance of tableting problems and provide a preferred starting materials for pharmaceuticals. These properties are neither disclosed nor suggested in Miura, Spanton or Bosch. There is nothing in any of the cited references, alone or in combination, that would lead one skilled in the art to predict the properties of Crystal Form D obtained by preparing Crystal Form D from Crystal form E.


Therefore, it is respectfully submitted that the processes recited in claims 25-27 are not obvious over Miura in view of Spanton and/or Bosch, and it is respectfully requested that the rejection of these claims be withdrawn. In addition, Crystal Form D recited in claims 26, 28 and 35 is not obvious over Miura in view of Spanton and Bosch for the same reasons.

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

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Respectfully submitted,

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